

# Supplementary Information

## Conditional and joint multiple SNP analysis of GWAS summary statistics identifies additional variants influencing complex traits

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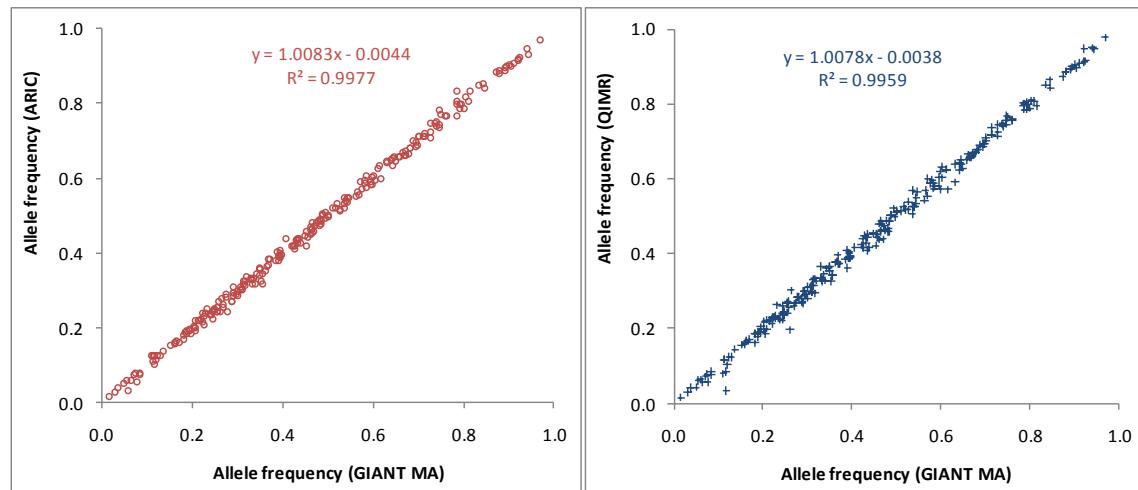
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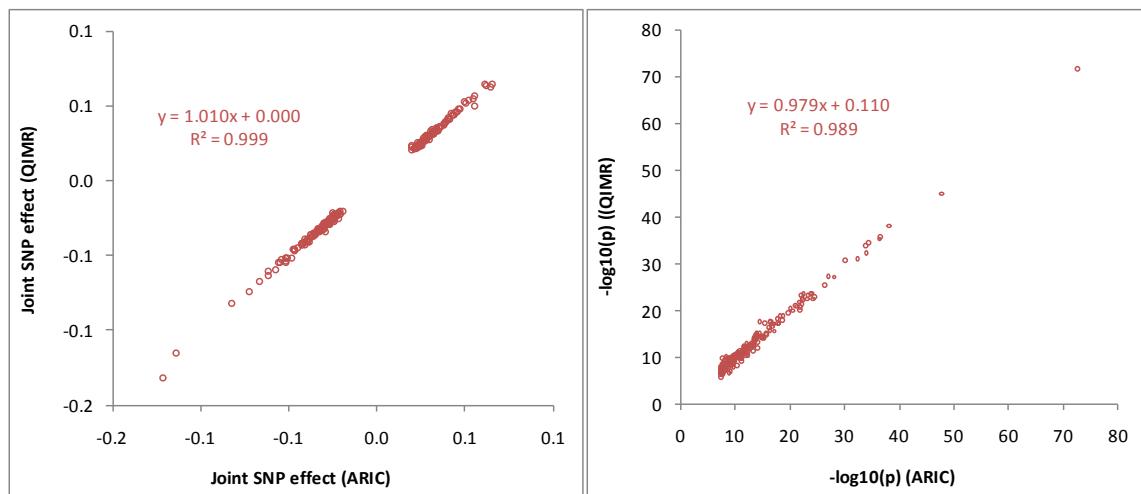
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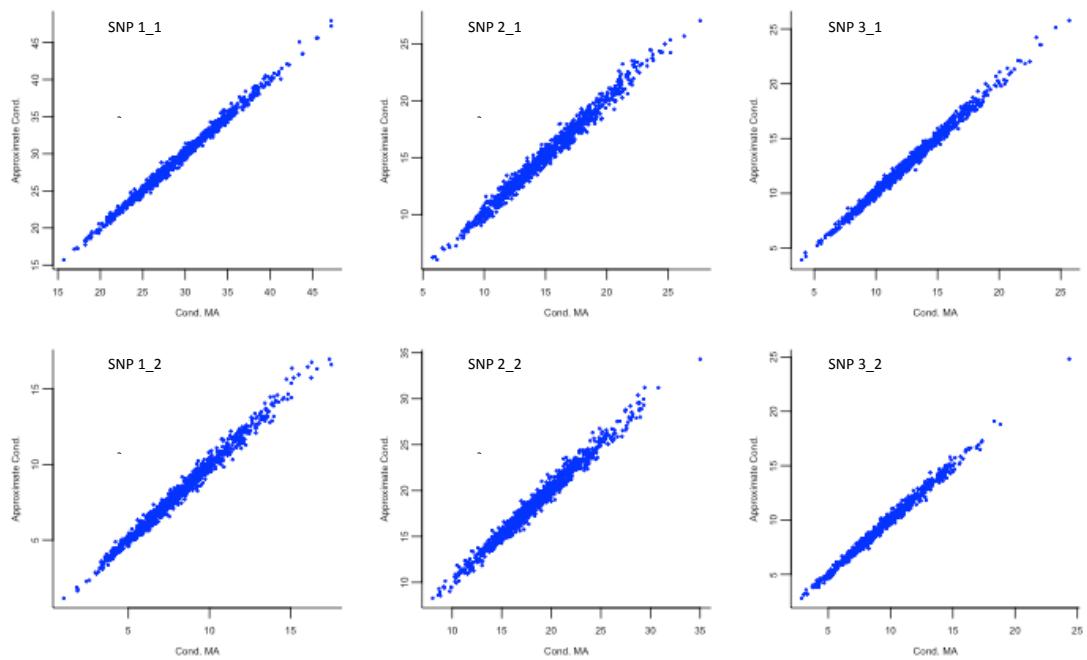
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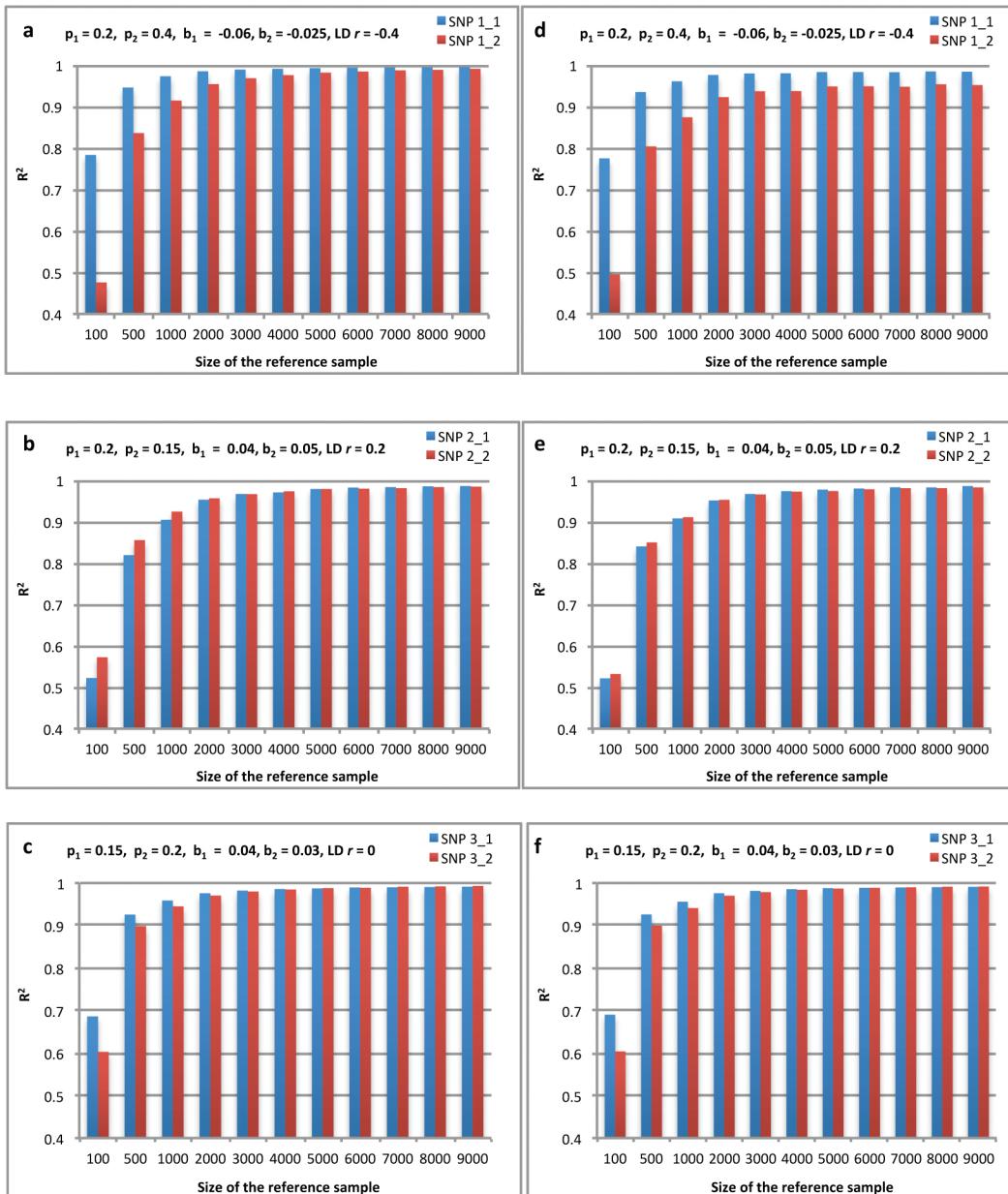
**Supplementary Figure 1** Allele frequencies estimated in the ARIC and QIMR cohorts against those reported by the GIANT MA for the 247 height-associated SNPs.



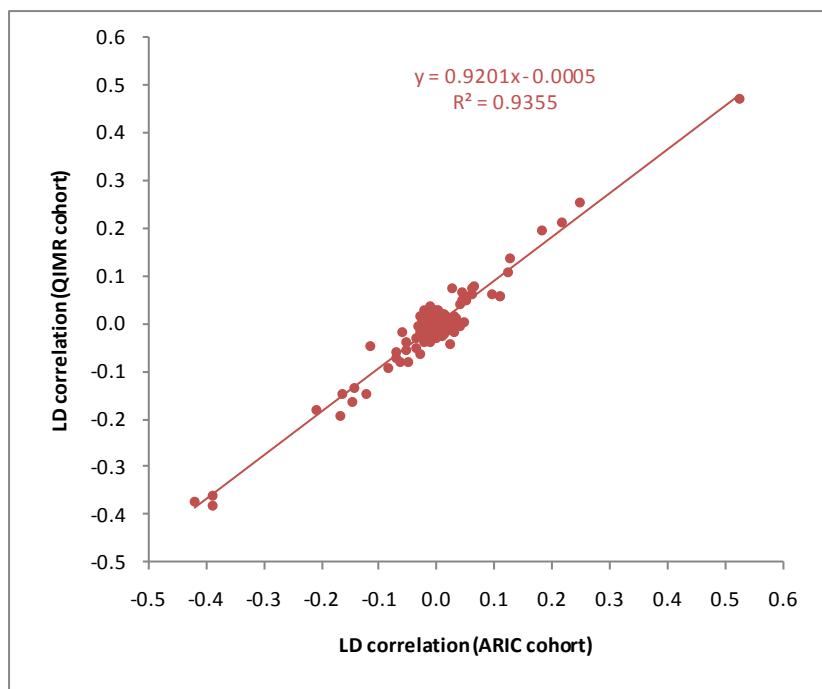
**Supplementary Figure 2** Effects and p-values of the 247 height-associated SNPs from the joint analysis using the QIMR cohort as reference sample against those using the ARIC cohort as reference sample.



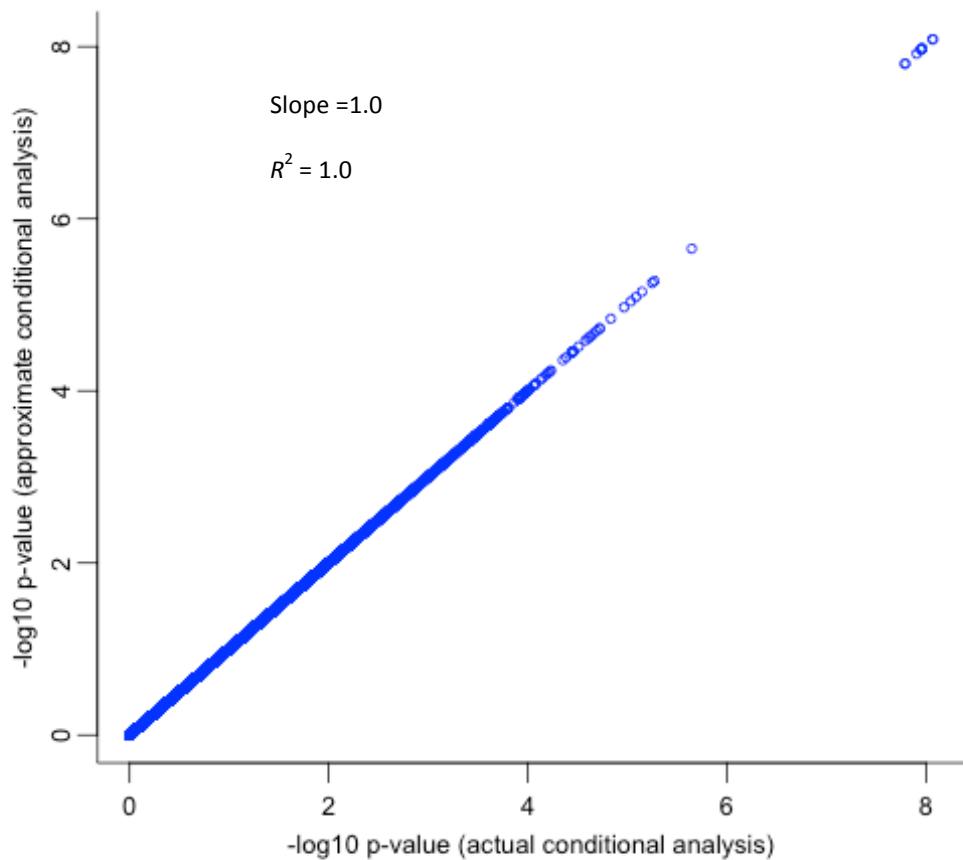
**Supplementary Figure 3** Plots of  $-\log_{10}$  p-values from the conditional MA against those from the approximate conditional analysis with a reference sample of 6,654 from 1,000 simulations. The simulation method and scheme can be found in the **Supplementary Note**. The simulation parameters with respect to effect sizes and allele frequencies of the SNPs are listed in **Supplementary Table 4**.



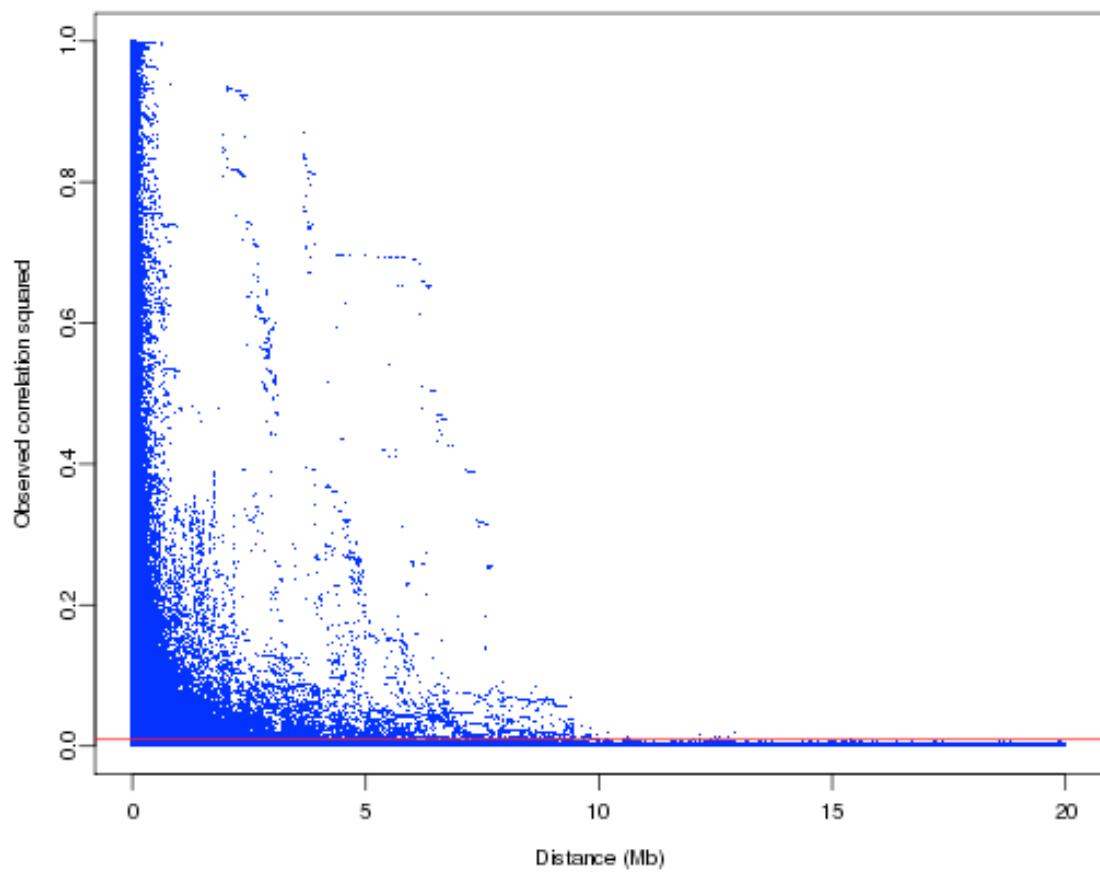
**Supplementary Figure 4** Squared correlations ( $R^2$ ) of  $-\log_{10} p\text{-value}$  between the conditional analysis with the actual genotype data and the approximate conditional analysis with different sizes of reference samples. In panels **a**, **b** and **c**, the reference sample is part of the discovery set. In panels **d**, **e** and **f**, the reference sample is independent of the discovery set. The simulation method and scheme can be found in the **Supplementary Note**. The simulation parameters with respect to effect sizes and allele frequencies of the SNPs are listed in **Supplementary Table 4**.



**Supplementary Figure 5** LD correlations between adjacent pairs of the 247 height-associated SNPs estimated in the ARIC cohort against those in the QIMR cohort.



**Supplementary Figure 6** Plot of p-values from the proposed method against those from the actual conditional analysis in the ARIC cohort with individual-level genotype data available. We firstly performed single-SNP association analyses of all the SNPs on chromosome 2. Using the summary statistics from the single SNP analyses and the ARIC cohort itself as the reference sample, we then implemented our method to perform association analyses conditioning on the 14 GIANT height SNPs on chromosome 2, and compared the p-values with those from the actual association analysis implemented in PLINK<sup>1</sup>. It is shown that with the individual-level genotype data of the discovery sample as the reference sample, our method is equivalent to a multiple regression analysis without any approximation.



**Supplementary Figure 7** Plot of the observed  $r^2$  (squared LD correlation) values between pairs of SNPs against their physical distances in the QIMR cohort. We randomly sampled 1,000 SNPs across the whole genome as target SNPs. For each target SNP, we calculated its  $r^2$  value with all the other SNPs in 20Mb distance in either direction. We then plotted the observed  $r^2$  values against the distances between the target SNPs and the other SNPs. The figure shows in general LD degrades exponentially with the increase of distance except for a number of outliers. The major outliers, e.g.  $r^2 > 0.4$  when distance  $> 2\text{Mb}$  and  $r^2 > 0.2$  when distance  $> 5\text{Mb}$ , are located at a small number of long-range LD regions identified by principal component analysis in a previous study (Table 1 of Price et al.<sup>2</sup>). When the distance is  $> 10\text{Mb}$ , the observed  $r^2$  values are consistent with what we would expect by chance (the red line, 95% CI adjusted for the number of calculations).

## Supplementary Tables

**Supplementary Table 1** Summary of numbers of SNPs in different categories

	Height ( $p < 5e-8$ )	BMI ( $p < 5e-8$ )	BMI ( $p < 5e-6$ )
Total number of associated SNPs	247	33	132
Number of associated SNPs for which adjacent associated SNPs at more than 1Mb distant	160	33	113
Number of associated SNPs for which adjacent associated SNPs at less than 1Mb distant	87 (at 36 loci <sup>1</sup> )	0	19 (at 9 loci <sup>1</sup> )
Number of Leading SNPs at the loci with multiple associated SNPs	38	0	9
<b>Number of additional SNPs at the loci with multiple associated SNPs</b>	<b>49</b>	<b>0</b>	<b>10</b>

<sup>1</sup> A locus is defined as a chromosomal region at which adjacent pairs of associated SNPs are less than 1Mb distant.

**Supplementary Table 2** Summary of 247 height-associated SNPs with p-values < 5e-8 identified by the conditional and joint analysis using the ARIC cohort as reference sample with their effects replicated by a joint analysis using the QIMR cohort as reference sample. A total of 36 loci with multiple associated SNPs are highlighted in gray or green. SNPs on different chromosomes or more than 10Mb distant are assumed to be in linkage equilibrium. Chr, chromosome; A1, reference allele; Freq: frequency of the reference allele;  $\beta$ , marginal effect;  $b$ , joint effect;  $r$ , LD correlation between an associated SNP and the next adjacent associated SNP.

SNP	Chr	bp	A1	GIANT MA				Joint analysis with LD from ARIC					Joint analysis with LD from QIMR				
				Freq	$\beta$	s.e	P	Freq	b	s.e	P	r	Freq	b	s.e	P	r
rs425277	1	2,059,032	T	.276	.024	.0042	1.0E-08	.289	.024	.0042	1.1E-08		.284	.024	.0042	1.1E-08	
rs2284746	1	17,179,262	C	.482	-.035	.0038	2.4E-20	.474	-.036	.0038	8.1E-21	.007	.469	-.036	.0038	3.1E-21	-.010
rs1738475	1	23,409,478	C	.594	.022	.0038	1.3E-08	.589	.021	.0038	1.8E-08	-.006	.583	.021	.0038	2.1E-08	.003
rs4601530	1	24,916,698	T	.256	-.024	.0042	1.8E-08	.254	-.024	.0042	6.7E-09	.029	.273	-.025	.0042	5.3E-09	-.016
rs7532866	1	26,614,131	A	.665	.022	.0040	3.4E-08	.667	.022	.0040	1.9E-08		.657	.022	.0040	2.9E-08	
rs2154319	1	41,518,357	T	.751	-.034	.0045	1.6E-13	.771	-.034	.0045	9.9E-14		.765	-.034	.0045	9.9E-14	
rs17391694	1	78,396,214	T	.112	.040	.0067	2.7E-09	.126	.040	.0067	2.6E-09		.117	.040	.0067	2.6E-09	
rs6699417	1	88,896,031	T	.617	.022	.0038	1.3E-08	.598	.021	.0038	1.7E-08	-.012	.572	.022	.0038	7.9E-09	.011
rs10874746	1	93,096,559	T	.372	-.022	.0038	1.8E-08	.384	-.021	.0038	1.7E-08		.372	-.022	.0038	7.9E-09	
rs12047268	1	103,246,082	C	.310	.025	.0041	1.5E-09	.300	.025	.0041	1.3E-09		.299	.025	.0041	1.3E-09	
rs17038182	1	118,669,928	C	.245	-.037	.0043	1.2E-17	.243	-.037	.0043	6.4E-18		.262	-.037	.0043	6.4E-18	
rs2120003	1	145,157,259	T	.128	-.032	.0056	1.0E-08	.126	-.032	.0056	1.1E-08	.007	.123	-.032	.0056	1.0E-08	.004
rs7534365	1	148,142,748	T	.815	-.040	.0056	1.9E-12	.835	-.039	.0056	2.0E-12		.796	-.040	.0056	1.8E-12	
rs12086448	1	158,660,529	A	.478	.022	.0038	1.6E-08	.487	.022	.0038	1.3E-08		.489	.022	.0038	1.3E-08	
rs17346452	1	170,319,910	T	.727	-.038	.0042	2.5E-19	.706	-.040	.0042	2.8E-21	.109	.715	-.039	.0042	1.2E-20	.059
rs2421992	1	170,507,874	T	.701	.021	.0045	2.6E-06	.713	.025	.0045	2.6E-08	-.002	.703	.023	.0045	3.7E-07	-.011
rs1325598	1	175,058,872	A	.428	-.026	.0038	1.1E-11	.436	-.025	.0038	2.4E-11	-.008	.449	-.025	.0038	4.6E-11	.013
rs9425569	1	181,208,825	A	.599	-.022	.0040	1.8E-08	.602	-.023	.0040	6.1E-09	-.013	.621	-.024	.0040	2.5E-09	-.039
rs1046934	1	182,290,152	A	.644	-.046	.0040	2.2E-30	.632	-.046	.0040	6.9E-31		.652	-.047	.0040	2.0E-31	
rs10863936	1	210,304,421	A	.537	-.022	.0037	3.7E-09	.518	-.022	.0037	1.4E-09	-.004	.525	-.021	.0037	1.0E-08	-.003
rs6684205	1	216,676,325	A	.714	-.033	.0041	1.6E-15	.711	-.035	.0041	1.9E-17	.051	.719	-.035	.0041	2.7E-17	.049
rs11118171	1	217,114,492	A	.631	.025	.0039	2.2E-10	.644	.025	.0039	2.4E-10	-.084	.640	.024	.0039	4.7E-10	-.093
rs11118346	1	217,810,342	T	.464	-.026	.0037	1.7E-12	.469	-.025	.0037	6.9E-12	-.009	.459	-.024	.0037	1.2E-10	-.006
rs12081818	1	225,886,997	T	.195	-.032	.0047	9.6E-12	.192	-.033	.0047	1.7E-12		.204	-.033	.0047	1.3E-12	
rs7601531	2	19,831,425	T	.585	.024	.0039	2.3E-09	.608	.023	.0039	2.7E-09	.010	.581	.023	.0039	3.9E-09	-.013
rs6731333	2	23,966,858	T	.189	-.025	.0048	2.0E-07	.194	-.027	.0048	3.3E-08	-.053	.192	-.024	.0048	4.5E-07	-.040
rs4665736	2	25,041,103	T	.535	.034	.0038	1.3E-18	.533	.029	.0038	3.7E-14	.123	.507	.029	.0038	2.2E-14	.109
rs11694842	2	25,336,474	A	.669	.028	.0040	2.6E-12	.660	.026	.0041	1.1E-10	-.009	.658	.025	.0040	2.8E-10	-.031
rs6714546	2	33,214,929	A	.280	-.025	.0045	2.2E-08	.241	-.025	.0045	3.4E-08	-.005	.283	-.022	.0045	1.5E-06	.016
rs17511102	2	37,814,117	A	.912	-.060	.0071	1.8E-17	.908	-.061	.0071	1.6E-17	.004	.909	-.061	.0071	6.4E-18	.029
rs2341459	2	44,621,706	T	.270	.028	.0042	5.4E-11	.264	.028	.0042	4.1E-11	.000	.261	.028	.0042	1.2E-11	.003
rs17822294	2	46,813,508	A	.350	.023	.0039	5.3E-09	.359	.024	.0039	1.7E-09	.016	.366	.025	.0039	1.0E-10	-.006
rs1367226	2	55,943,044	A	.434	-.005	.0038	2.0E-01	.428	-.027	.0042	5.0E-11	-.421	.409	-.024	.0041	5.0E-09	-.375
rs3791675	2	55,964,813	T	.234	-.050	.0045	1.1E-28	.249	-.063	.0050	3.0E-37		.228	-.061	.0049	1.5E-36	
rs11684404	2	88,705,737	T	.674	-.027	.0039	7.5E-12	.659	-.027	.0039	4.5E-12		.665	-.027	.0039	4.5E-12	
rs2166898	2	121,329,129	A	.161	-.029	.0052	2.9E-08	.161	-.029	.0052	3.8E-08		.159	-.029	.0052	3.8E-08	
rs7567288	2	134,151,294	T	.804	-.031	.0048	1.1E-10	.817	-.031	.0048	1.2E-10		.811	-.031	.0048	1.2E-10	
rs7567851	2	178,392,966	C	.085	.041	.0070	4.0E-09	.078	.041	.0070	3.7E-09		.075	.041	.0070	3.7E-09	
rs1351164	2	217,980,143	T	.786	.028	.0046	1.6E-09	.807	.028	.0046	1.5E-09	-.002	.802	.028	.0046	6.1E-10	.002
rs1541777	2	219,295,535	A	.526	.025	.0037	1.0E-11	.513	.022	.0037	6.4E-09	.062	.517	.022	.0037	4.6E-09	.076
rs6741325	2	219,615,943	C	.902	.048	.0063	2.0E-14	.902	.044	.0063	5.2E-12	.060	.904	.043	.0063	6.4E-12	.063
rs16859517	2	219,657,428	T	.036	.073	.0107	5.8E-12	.038	.064	.0108	2.6E-09	-.005	.042	.065	.0107	1.1E-09	.010
rs2629046	2	224,755,988	T	.547	.025	.0037	4.3E-11	.549	.026	.0037	5.3E-12	.023	.565	.024	.0037	4.5E-11	.000
rs7598759	2	232,030,200	T	.454	-.022	.0040	6.2E-08	.419	-.023	.0040	1.2E-08	-.013	.422	-.021	.0040	1.1E-07	-.015
rs2580816	2	232,506,210	T	.197	-.041	.0049	7.3E-17	.185	-.041	.0049	2.7E-17	-.016	.188	-.043	.0049	2.3E-18	.004
rs7571716	2	233,149,664	T	.292	.028	.0041	7.1E-12	.287	.027	.0041	3.6E-11	.008	.299	.028	.0041	1.1E-11	-.015
rs4676386	2	241,423,659	A	.483	.023	.0038	1.5E-09	.477	.022	.0038	5.7E-09	-.028	.460	.024	.0038	2.9E-10	-.019
rs12694997	2	241,911,659	A	.244	-.027	.0044	5.4E-10	.234	-.027	.0044	6.2E-10		.222	-.026	.0044	2.2E-09	
rs6772112	3	11,616,535	T	.940	.046	.0080	1.1E-08	.944	.046	.0080	6.5E-09	.012	.950	.046	.0080	1.0E-08	.001
rs2597513	3	13,530,836	T	.894	-.039	.0062	1.9E-10	.901	-.040	.0062	1.6E-10		.899	-.039	.0062	2.5E-10	
rs13088462	3	51,046,753	T	.943	-.054	.0089	1.1E-09	.932	-.053	.0089	3.7E-09	.031	.947	-.054	.0089	1.1E-09	-.003
rs2336725	3	53,093,779	T	.544	-.026	.0040	3.0E-11	.549	-.026	.0040	1.4E-10	.004	.549	-.026	.0040	4.2E-11	.001

rs4681933	3	56,635,269	A	.541	.022	.0037	6.8E-09	.541	.022	.0037	4.2E-09	.527	.022	.0037	5.1E-09		
rs17806888	3	67,499,012	T	.881	.040	.0063	1.7E-10	.887	.039	.0063	4.8E-10	.018	.887	.039	.0063	6.6E-10	-.026
rs9863706	3	72,520,103	T	.216	-.030	.0045	2.2E-11	.221	-.030	.0045	2.9E-11	.222	-.030	.0045	3.9E-11		
rs2718423	3	115,691,287	T	.170	-.028	.0051	3.8E-08	.162	-.028	.0051	4.5E-08	.172	-.028	.0051	4.5E-08		
rs6439167	3	130,533,446	T	.214	-.034	.0046	1.3E-13	.220	-.034	.0046	7.5E-14	-.020	.222	-.033	.0046	6.6E-13	.025
rs9844666	3	137,456,906	A	.255	-.028	.0043	5.7E-11	.242	-.029	.0043	8.7E-12	-.004	.242	-.027	.0043	6.4E-10	.014
rs724016	3	142,588,260	A	.569	-.067	.0037	1.1E-72	.556	-.067	.0037	2.4E-73	.555	-.067	.0037	1.8E-72		
rs9818941	3	159,169,151	A	.740	-.027	.0043	4.3E-10	.751	-.027	.0043	6.2E-10	.744	-.027	.0043	6.2E-10		
rs7652177	3	173,451,771	C	.496	-.031	.0037	3.9E-16	.491	-.029	.0037	1.2E-14	-.060	.497	-.030	.0037	5.4E-16	-.016
rs572169	3	173,648,421	T	.313	.036	.0040	1.0E-18	.315	.034	.0040	4.8E-17	.315	.035	.0040	2.3E-18		
rs6784185	3	186,955,759	A	.203	-.008	.0046	8.8E-02	.205	-.034	.0053	2.2E-10	.523	.200	-.029	.0051	1.0E-08	.470
rs720390	3	187,031,377	A	.386	.031	.0040	1.8E-14	.378	.045	.0046	1.5E-22	.384	.042	.0045	6.7E-21		
rs3958122	4	1,663,729	T	.357	.025	.0039	1.7E-10	.343	.025	.0039	1.0E-10	.341	.025	.0039	1.0E-10		
rs763318	4	12,572,672	A	.465	-.020	.0037	9.0E-08	.464	-.021	.0037	1.7E-08	.011	.463	-.019	.0037	1.5E-07	.004
rs16896276	4	17,624,254	A	.269	.041	.0042	8.2E-23	.256	.030	.0043	1.8E-12	.248	.267	.030	.0043	3.5E-12	.256
rs2061455	4	17,644,348	A	.847	.072	.0055	7.8E-39	.841	.063	.0057	7.2E-29	.843	.062	.0057	7.6E-28		
rs17081935	4	57,518,233	T	.193	.031	.0047	7.5E-11	.194	.031	.0047	7.5E-11	.191	.031	.0047	7.5E-11		
rs7697556	4	73,734,177	T	.476	.022	.0038	7.2E-09	.481	.022	.0038	8.6E-09	.001	.463	.022	.0038	6.7E-09	-.004
rs7661369	4	82,385,090	A	.316	.038	.0040	2.3E-21	.312	.038	.0040	1.1E-21	.294	.038	.0040	8.5E-22		
rs2101975	4	106,436,116	A	.584	.022	.0038	2.1E-08	.573	.022	.0038	1.5E-08	.575	.022	.0038	1.5E-08		
rs6824258	4	122,989,417	T	.728	-.025	.0043	4.2E-09	.745	-.025	.0043	5.3E-09	.745	-.025	.0043	5.3E-09		
rs17720281	4	145,763,226	T	.406	.047	.0041	1.7E-30	.437	.031	.0044	9.2E-13	-.389	.417	.032	.0044	9.2E-14	-.360
rs7689420	4	145,787,802	T	.163	-.069	.0051	1.1E-41	.164	-.054	.0055	2.9E-23	.167	-.055	.0054	3.0E-24		
rs955748	4	184,452,669	A	.246	-.024	.0043	1.7E-08	.243	-.024	.0043	1.6E-08	.246	-.024	.0043	1.6E-08		
rs7731703	5	32,730,699	T	.312	-.030	.0047	1.4E-10	.324	-.032	.0047	1.4E-11	.143	.332	-.030	.0047	1.5E-10	-.134
rs1173735	5	32,807,136	A	.739	-.030	.0042	1.3E-12	.738	-.042	.0043	5.1E-23	.181	.740	-.043	.0043	5.4E-23	.198
rs1173727	5	32,866,278	T	.394	.036	.0038	1.5E-20	.409	.040	.0039	1.4E-24	-.071	.403	.040	.0039	2.5E-24	-.072
rs11745439	5	33,265,791	A	.288	-.028	.0042	1.3E-11	.271	-.026	.0042	9.9E-10	.271	-.025	.0042	1.5E-09		
rs7716219	5	54,990,828	T	.301	.028	.0040	4.0E-12	.296	.028	.0040	2.6E-12	.311	.028	.0040	2.6E-12		
rs34651	5	72,179,761	T	.922	-.045	.0073	6.1E-10	.919	-.045	.0073	7.8E-10	.913	-.045	.0073	7.8E-10		
rs10037512	5	88,390,431	T	.563	.027	.0038	3.0E-12	.553	.027	.0038	2.1E-12	.544	.027	.0038	2.1E-12		
rs13177718	5	108,141,243	T	.075	-.041	.0075	3.7E-08	.078	-.041	.0075	4.0E-08	.078	-.041	.0075	4.0E-08		
rs1582931	5	122,685,098	A	.471	-.025	.0038	2.3E-11	.472	-.025	.0038	3.0E-11	.005	.474	-.026	.0038	1.9E-11	-.005
rs274546	5	131,727,766	A	.390	-.028	.0038	3.7E-13	.389	-.028	.0038	7.2E-14	-.028	.362	-.028	.0038	4.6E-13	.015
rs537930	5	134,376,602	T	.256	-.031	.0043	9.7E-13	.254	-.032	.0043	1.5E-13	.270	-.030	.0043	1.5E-12		
rs4282339	5	168,188,818	A	.203	-.035	.0047	5.9E-14	.199	-.036	.0047	2.1E-14	-.005	.217	-.037	.0047	2.6E-15	.011
rs4620037	5	170,807,702	A	.801	.032	.0046	3.6E-12	.788	.035	.0046	4.2E-14	.049	.790	.034	.0046	2.6E-13	.058
rs1529701	5	170,933,582	T	.292	-.023	.0042	4.9E-08	.309	-.024	.0042	1.6E-08	.001	.299	-.025	.0042	2.0E-09	-.025
rs12153391	5	171,136,043	A	.255	-.033	.0045	2.4E-13	.244	-.033	.0045	4.3E-13	.027	.267	-.030	.0045	3.6E-11	.073
rs4868126	5	171,216,074	T	.396	-.031	.0042	3.3E-13	.397	-.030	.0042	6.8E-13	-.002	.393	-.030	.0042	8.8E-13	-.032
rs6556079	5	172,929,684	A	.603	-.029	.0038	1.0E-13	.593	-.028	.0038	6.6E-14	.007	.603	-.028	.0038	1.7E-13	.014
rs422421	5	176,449,932	T	.220	-.033	.0046	5.2E-13	.225	-.033	.0046	5.6E-13	.018	.213	-.031	.0046	1.0E-11	.007
rs6879260	5	179,663,620	T	.393	-.028	.0038	2.3E-13	.388	-.028	.0038	2.0E-13	.403	-.027	.0038	1.2E-12		
rs4246079	6	6,834,817	A	.118	-.039	.0065	1.9E-09	.124	-.039	.0065	2.5E-09	.001	.034	-.041	.0065	2.6E-10	-.020
rs3812163	6	7,670,759	A	.540	-.037	.0038	5.3E-22	.541	-.037	.0038	1.7E-22	.023	.526	-.036	.0038	2.2E-21	-.044
rs9942510	6	7,745,305	A	.162	.029	.0051	1.3E-08	.156	.030	.0051	4.3E-09	.164	.028	.0051	5.9E-08		
rs1047014	6	19,949,472	T	.747	-.029	.0046	2.7E-10	.744	-.030	.0046	1.1E-10	.011	.746	-.030	.0046	5.3E-11	.021
rs806794	6	26,308,656	A	.714	.053	.0042	1.9E-35	.718	.052	.0042	1.0E-34	-.036	.738	.050	.0042	4.4E-33	-.051
rs1265097	6	31,214,438	A	.118	-.055	.0063	2.9E-18	.103	-.054	.0063	7.4E-18	-.017	.085	-.052	.0063	2.3E-16	.014
rs1061807	6	32,244,816	A	.261	-.033	.0044	1.3E-13	.245	-.031	.0044	2.6E-12	.008	.197	-.032	.0044	5.9E-13	.004
rs12204421	6	33,736,841	A	.738	.030	.0044	5.6E-12	.747	.030	.0044	1.0E-11	.001	.748	.029	.0044	4.2E-11	.021
rs12214804	6	34,296,844	T	.925	-.079	.0075	3.5E-26	.922	-.082	.0075	9.9E-28	.064	.916	-.083	.0075	5.6E-28	.078
rs3800461	6	34,724,300	C	.124	.045	.0057	6.4E-15	.126	.046	.0057	7.3E-16	-.054	.124	.044	.0057	8.3E-15	-.055
rs6899744	6	35,394,273	T	.016	-.138	.0174	2.2E-15	.018	-.131	.0175	5.5E-14	-.009	.015	-.121	.0175	4.1E-12	-.010
rs9296450	6	45,061,764	T	.786	.031	.0046	3.0E-11	.798	.030	.0046	4.4E-11	.015	.794	.030	.0046	4.4E-11	
rs9360921	6	76,322,362	T	.890	-.048	.0061	2.6E-15	.888	-.047	.0061	2.1E-14	-.023	.892	-.046	.0061	2.7E-14	-.022
rs648831	6	81,012,927	T	.493	.028	.0038	2.7E-13	.509	.025	.0038	3.5E-11	-.064	.521	.025	.0038	7.1E-11	-.081
rs310402	6	81,857,211	T	.462	-.030	.0037	2.6E-15	.452	-.028	.0037	5.6E-14	.438	-.027	.0037	1.8E-13		
rs314263	6	105,499,438	T	.678	-.041	.0040	1.7E-24	.664	-.041	.0040	1.1E-24	.001	.669	-.041	.0040	2.1E-24	-.009
rs3734652	6	109,893,673	T	.583	.022	.0038	4.2E-09	.586	.022	.0038	5.0E-09	-.006	.590	.022	.0038	6.2E-09	.005
rs961764	6	117,628,849	C	.424	-.023	.0037	1.1E-09	.418	-.023	.0037	9.9E-10	-.002	.418	-.024	.0037	1.1E-10	.027
rs1490384	6	126,892,853	T	.500	.037	.0038	7.9E-23	.499	.037	.0038	6.0E-23	.013	.512	.038	.0038	2.8E-23	.001
rs6569648	6	130,390,812	T	.761	-.036	.0044	3.7E-16	.768	-.036	.0044	2.4E-16	-.011	.756	-.035	.0044	8.1E-16	-.017
rs65692107	6	131,369,649	A	.366	.021	.0039	3.0E-08	.362	.021	.0039	4.9E-08	.379	.021	.0039	6.6E-08		
rs262115	6	142,859,100	T	.698	.044	.0041	3.3E-26	.687	.044	.0041	3.9E-27	.002	.695	.043	.0041	3.5E-2	

rs12538581	7	20,365,642	A	.502	-.024	.0038	4.7E-10	.497	-.024	.0038	1.5E-10	-.005	.514	-.024	.0038	5.1E-10	-.014
rs6957923	7	23,449,210	A	.368	-.025	.0038	1.9E-10	.385	-.024	.0038	1.6E-10	.008	.395	-.025	.0038	4.9E-11	.003
rs537124	7	28,169,667	T	.701	-.042	.0041	2.2E-24	.711	-.043	.0041	3.1E-25	-.021	.711	-.041	.0041	1.3E-23	-.001
rs6959212	7	38,094,851	T	.319	-.023	.0041	1.7E-08	.336	-.023	.0041	1.1E-08	.015	.328	-.023	.0041	3.9E-08	.016
rs12534698	7	46,374,789	A	.083	-.043	.0069	5.6E-10	.075	-.042	.0069	7.9E-10		.085	-.042	.0069	8.1E-10	
rs42235	7	92,086,012	T	.312	.055	.0042	7.1E-39	.303	.055	.0042	7.3E-39		.316	.055	.0042	7.3E-39	
rs822552	7	148,281,567	C	.747	-.030	.0048	2.3E-10	.736	-.030	.0048	5.1E-10	.010	.758	-.030	.0048	4.4E-10	.007
rs2110001	7	150,147,955	C	.696	-.033	.0045	2.7E-13	.683	-.033	.0045	5.1E-13		.695	-.033	.0045	4.4E-13	
rs1013209	8	24,172,249	T	.248	-.029	.0044	1.1E-10	.248	-.029	.0044	7.0E-11		.237	-.029	.0044	7.0E-11	
rs10958476	8	57,258,362	T	.787	-.042	.0048	1.4E-18	.833	-.036	.0049	1.6E-13	-.167	.785	-.035	.0049	1.0E-12	-.194
rs7460090	8	57,356,717	T	.873	.055	.0057	8.6E-22	.882	.047	.0058	2.2E-16	.008	.874	.046	.0058	1.6E-15	.019
rs4738736	8	59,998,555	T	.337	.023	.0040	5.3E-09	.333	.023	.0040	9.5E-09		.345	.022	.0040	2.2E-08	
rs6473015	8	78,341,040	A	.713	-.032	.0042	1.4E-14	.713	-.032	.0042	2.6E-14		.719	-.032	.0042	2.6E-14	
rs16892729	8	120,627,259	T	.243	-.025	.0044	7.3E-09	.233	-.025	.0044	7.8E-09		.241	-.025	.0044	7.8E-09	
rs6470764	8	130,794,847	T	.208	-.047	.0047	5.3E-23	.198	-.046	.0047	6.9E-23	.017	.199	-.047	.0047	6.3E-24	-.014
rs11785144	8	135,685,381	T	.395	-.030	.0038	5.4E-15	.391	-.029	.0038	1.6E-14		.389	-.030	.0038	1.4E-15	
rs7864648	9	16,358,732	T	.317	.025	.0041	3.3E-09	.325	.025	.0041	2.0E-09		.333	.025	.0041	2.0E-09	
rs11144688	9	77,732,106	A	.111	-.055	.0076	6.3E-13	.125	-.054	.0076	7.8E-13	.009	.080	-.055	.0076	3.1E-13	-.017
rs930340	9	85,853,334	A	.793	-.027	.0048	2.0E-08	.799	-.027	.0048	2.0E-08	.002	.806	-.029	.0048	2.1E-09	-.022
rs465228	9	88,274,340	A	.488	-.023	.0037	4.6E-10	.502	-.024	.0037	7.3E-11	.029	.502	-.024	.0037	9.5E-11	.015
rs4877418	9	90,026,318	T	.238	-.027	.0044	1.5E-09	.235	-.028	.0044	1.9E-10	.000	.225	.026	.0044	2.1E-09	-.011
rs9969804	9	94,468,941	A	.434	.028	.0038	8.2E-14	.438	-.029	.0038	2.8E-14	-.029	.443	.029	.0038	1.2E-14	-.009
rs473902	9	97,296,056	T	.922	-.074	.0081	7.0E-20	.913	-.064	.0082	7.3E-15	-.208	.948	.062	.0082	6.6E-14	-.183
rs10512248	9	97,299,524	T	.660	-.033	.0040	1.5E-16	.658	-.026	.0041	1.2E-10	-.020	.665	-.027	.0041	4.4E-11	-.022
rs10990303	9	97,450,226	T	.227	.030	.0046	1.4E-10	.208	.029	.0046	2.4E-10	.033	.235	.027	.0046	2.5E-09	.010
rs2025151	9	98,201,333	C	.810	-.041	.0050	3.1E-16	.806	-.041	.0050	5.0E-16		.807	-.039	.0050	5.3E-15	
rs7027110	9	108,638,867	A	.227	.034	.0044	2.2E-14	.230	.034	.0044	2.5E-14	-.008	.226	.034	.0044	1.3E-14	.002
rs1468758	9	112,846,903	T	.249	-.026	.0045	9.1E-09	.252	-.026	.0045	1.0E-08	.003	.245	-.027	.0045	1.8E-09	.001
rs13302480	9	117,505,134	C	.115	-.036	.0062	7.2E-09	.109	-.037	.0062	1.9E-09	.041	.118	-.037	.0062	2.4E-09	.040
rs7869550	9	118,174,617	A	.796	.030	.0046	1.5E-10	.799	.031	.0046	1.6E-11		.799	.032	.0046	3.2E-12	
rs7466269	9	132,453,905	A	.642	.036	.0039	7.9E-20	.652	.035	.0039	1.6E-19	.015	.642	.035	.0039	1.6E-19	.009
rs7849585	9	138,251,691	T	.334	.032	.0041	4.6E-15	.318	.031	.0041	3.7E-14	-.031	.330	.032	.0041	7.6E-15	-.007
rs8413	9	138,443,132	T	.599	-.026	.0039	3.0E-11	.584	-.024	.0039	4.2E-10		.572	-.025	.0039	1.9E-10	
rs7909670	10	12,958,770	T	.432	-.022	.0038	7.3E-09	.435	-.022	.0038	8.3E-09		.429	-.022	.0038	8.3E-09	
rs779933	10	80,588,523	A	.439	-.023	.0038	2.1E-09	.426	-.024	.0038	3.6E-10	-.037	.417	-.024	.0038	4.6E-10	-.031
rs2145998	10	80,791,702	A	.480	-.025	.0038	2.0E-11	.490	-.026	.0038	7.2E-12		.458	-.026	.0038	9.2E-12	
rs11599750	10	101,795,432	T	.389	-.023	.0039	3.3E-09	.401	-.023	.0039	3.7E-09		.409	-.023	.0039	3.7E-09	
rs234886	11	2,758,666	C	.892	-.043	.0065	3.5E-11	.896	-.042	.0065	7.6E-11	.026	.894	-.043	.0065	4.5E-11	.012
rs7937898	11	12,660,137	T	.543	-.024	.0037	1.7E-10	.537	-.023	.0037	4.3E-10	-.009	.535	-.024	.0037	7.5E-11	.022
rs1330	11	17,272,605	T	.350	.024	.0040	1.4E-09	.339	.024	.0040	2.4E-09		.354	.025	.0040	7.4E-10	
rs10838801	11	48,054,856	A	.694	-.031	.0041	1.5E-14	.697	-.031	.0041	2.8E-14		.686	-.031	.0041	2.8E-14	
rs3782089	11	65,093,395	T	.060	-.058	.0084	5.0E-12	.033	-.060	.0084	1.2E-12	.022	.064	-.057	.0084	8.5E-12	-.015
rs634552	11	74,959,700	T	.137	.041	.0057	4.5E-13	.138	.042	.0057	1.6E-13		.145	.041	.0057	1.1E-12	
rs2510897	11	118,149,792	A	.576	-.021	.0038	6.8E-08	.573	-.021	.0038	3.8E-08	.013	.589	-.021	.0038	6.1E-08	-.001
rs654723	11	128,091,365	A	.612	.024	.0040	3.1E-09	.628	.024	.0040	2.0E-09		.625	.024	.0040	3.2E-09	
rs2856321	12	11,747,040	A	.641	-.030	.0039	2.6E-14	.650	-.030	.0039	1.2E-14	.009	.624	-.030	.0039	7.3E-15	.018
rs10770705	12	20,748,734	A	.329	.031	.0040	8.5E-15	.327	.032	.0040	1.0E-15	-.012	.366	.032	.0040	3.4E-15	.013
rs2638953	12	28,425,682	C	.683	.036	.0040	4.4E-19	.680	.036	.0040	2.5E-19		.677	.035	.0040	1.4E-18	
rs703830	12	54,988,139	T	.072	.052	.0075	6.2E-12	.075	.053	.0075	1.4E-12	.004	.072	.050	.0075	2.9E-11	-.006
rs17122670	12	58,263,968	A	.120	.033	.0061	3.5E-08	.114	.034	.0061	2.5E-08	-.008	.103	.032	.0061	2.3E-07	.018
rs1351394	12	64,638,093	T	.487	.054	.0037	2.3E-46	.504	.054	.0037	1.8E-48	-.007	.503	.053	.0037	9.7E-46	.004
rs10748128	12	68,113,925	T	.356	.035	.0044	1.8E-15	.317	.035	.0044	1.4E-15		.342	.034	.0044	7.8E-15	
rs17783015	12	88,755,517	T	.152	-.035	.0052	3.0E-11	.154	-.036	.0052	2.6E-12	.016	.156	-.037	.0052	7.3E-13	.008
rs11107116	12	92,502,635	T	.223	.052	.0044	4.0E-32	.216	.056	.0044	4.2E-37	.095	.230	.055	.0044	5.3E-36	.061
rs2885691	12	92,646,350	T	.436	-.029	.0038	2.3E-14	.439	-.034	.0038	1.1E-18	-.006	.454	-.033	.0038	7.3E-18	-.003
rs7971536	12	100,897,919	A	.465	-.025	.0039	3.6E-10	.455	-.024	.0039	3.4E-10		.486	-.025	.0039	7.7E-11	
rs7980687	12	122,388,664	A	.206	.036	.0047	6.7E-14	.192	.034	.0047	4.0E-13	.045	.186	.034	.0047	5.2E-13	.050
rs1809889	12	123,367,179	T	.290	.032	.0044	1.1E-12	.293	.030	.0044	7.7E-12		.268	.030	.0044	1.0E-11	
rs7327412	13	32,246,568	A	.448	.024	.0037	1.3E-10	.447	.024	.0037	7.4E-11		.454	.024	.0037	7.4E-11	
rs3118905	13	50,003,335	A	.288	-.052	.0042	2.0E-35	.269	-.052	.0042	3.6E-35		.282	-.052	.0042	3.6E-35	
rs7319045	13	90,822,575	A	.392	.029	.0039	6.4E-14	.378	.029	.0039	1.1E-13		.391	.029	.0039	1.1E-13	
rs1950500	14	23,900,690	T	.297	.032	.0041	2.4E-15	.290	.032	.0041	3.4E-15		.291	.032	.0041	3.4E-15	
rs2093210	14	60,027,032	T	.571	-.034	.0041	3.4E-17	.592	-.034	.0041	4.6E-17	-.006	.601	-.034	.0041	1.8E-16	.026
rs1980850	14	67,716,941	A	.182	-.027	.0050	5.1E-08	.167	-.028	.							

rs12440667	15	72,018,492	T	.467	-.028	.0039	1.4E-12	.481	-.030	.0039	2.2E-14	-.051	.481	-.031	.0039	4.8E-15	-.079
rs5742915	15	72,123,686	T	.527	-.031	.0041	8.2E-14	.516	-.032	.0041	3.4E-15	.539	-.033	.0041	7.9E-16		
rs11259936	15	82,371,586	A	.484	-.042	.0037	1.4E-29	.484	-.038	.0038	7.5E-24	-.164	.485	-.037	.0037	3.4E-23	-.147
rs12148239	15	82,432,022	T	.728	.031	.0042	1.1E-13	.724	.024	.0043	8.8E-09	.011	.727	.025	.0042	5.0E-09	.000
rs4932429	15	87,164,536	C	.510	-.025	.0039	2.7E-10	.520	-.022	.0039	2.3E-08	.047	.514	-.025	.0039	1.8E-10	.002
rs16942341	15	87,189,909	T	.031	-.134	.0131	2.2E-24	.027	-.116	.0132	1.8E-18	-.122	.030	-.114	.0132	5.6E-18	-.149
rs2280470	15	87,196,630	A	.334	.039	.0040	1.5E-22	.330	.036	.0040	6.3E-19	.010	.327	.036	.0040	1.7E-19	-.026
rs2871865	15	97,012,419	C	.880	.054	.0063	3.0E-17	.881	.050	.0063	3.5E-15	-.015	.887	.055	.0063	1.9E-18	-.004
rs12916269	15	98,347,739	A	.426	-.028	.0039	9.8E-13	.409	-.030	.0039	9.6E-15	-.069	.439	-.031	.0039	4.0E-15	-.060
rs2035344	15	98,507,671	A	.687	-.024	.0042	1.6E-08	.699	-.024	.0042	1.9E-08	.049	.691	-.024	.0042	1.9E-08	.051
rs4965598	15	98,577,137	T	.681	-.035	.0040	1.4E-18	.680	-.035	.0040	1.9E-18		.680	-.036	.0040	5.6E-19	
rs11648796	16	732,191	A	.748	-.031	.0050	8.1E-10	.780	-.030	.0050	1.3E-09	-.015	.768	-.031	.0050	8.5E-10	-.004
rs26868	16	2,189,377	A	.470	.030	.0045	5.6E-11	.459	.029	.0045	8.6E-11		.439	.030	.0045	5.6E-11	
rs1659127	16	14,295,806	A	.340	.024	.0043	2.9E-08	.318	.024	.0043	2.4E-08		.328	.024	.0043	2.4E-08	
rs8052560	16	87,304,743	A	.787	.039	.0058	2.1E-11	.768	.039	.0058	1.4E-11		.798	.039	.0058	1.4E-11	
rs4640244	17	21,224,816	A	.613	.028	.0045	7.1E-10	.633	.028	.0045	8.2E-10	.007	.625	.028	.0045	3.5E-10	.002
rs871014	17	24,969,465	T	.521	.019	.0038	4.6E-07	.532	.023	.0038	1.3E-09	.110	.518	.020	.0038	2.4E-07	.059
rs3764419	17	26,188,149	A	.392	-.037	.0039	2.7E-22	.390	-.040	.0039	6.2E-25	-.015	.386	-.039	.0039	3.5E-23	-.016
rs554078	17	27,354,222	A	.845	-.034	.0052	9.4E-11	.851	-.035	.0052	3.1E-11	-.001	.865	-.034	.0052	6.6E-11	.024
rs2338115	17	34,183,104	T	.535	.021	.0037	1.2E-08	.546	.022	.0037	2.9E-09	.004	.568	.021	.0037	8.3E-09	.004
rs507564	17	35,841,019	T	.183	-.028	.0050	2.2E-08	.188	-.028	.0050	1.9E-08	.001	.187	-.027	.0050	1.1E-07	.000
rs4986172	17	40,571,807	T	.353	-.028	.0041	2.9E-12	.325	-.029	.0041	1.7E-12	.003	.326	-.028	.0041	1.6E-11	-.009
rs1812364	17	44,373,024	A	.461	.023	.0037	7.8E-10	.462	.021	.0037	6.8E-09	.044	.481	.021	.0037	1.3E-08	.065
rs2072153	17	44,745,013	C	.306	.026	.0041	7.4E-11	.308	.026	.0041	4.6E-10	-.010	.311	.024	.0041	2.6E-09	-.002
rs4605213	17	46,599,746	C	.341	.023	.0040	4.1E-09	.344	.023	.0040	4.4E-09	-.004	.360	.024	.0040	1.2E-09	.010
rs227724	17	52,133,816	A	.657	-.027	.0040	7.0E-12	.656	-.026	.0040	6.9E-11	-.029	.651	-.026	.0040	5.5E-11	-.063
rs4794665	17	52,205,328	A	.485	.024	.0037	2.0E-10	.490	.023	.0037	7.5E-10	-.003	.488	.020	.0037	9.9E-08	.022
rs2079795	17	56,851,431	T	.329	.040	.0040	4.0E-23	.331	.039	.0040	6.4E-23	-.005	.335	.039	.0040	4.6E-22	-.004
rs12451513	17	56,997,110	T	.602	-.022	.0041	2.0E-07	.605	-.022	.0041	4.2E-08	.018	.633	-.021	.0041	2.3E-07	.003
rs2137143	17	59,159,133	T	.055	.049	.0088	3.1E-08	.059	.062	.0089	2.8E-12	-.147	.061	.064	.0089	5.6E-13	-.166
rs2727300	17	59,319,130	A	.275	.037	.0042	4.1E-18	.281	.041	.0042	4.7E-22	-.006	.269	.041	.0043	1.2E-21	.003
rs11867479	17	65,601,802	T	.348	.024	.0040	2.9E-09	.356	.023	.0040	6.6E-09	-.008	.363	.025	.0040	3.8E-10	-.017
rs2158917	17	67,437,704	T	.258	.024	.0043	1.5E-08	.269	.025	.0043	9.7E-09	-.023	.255	.024	.0043	2.1E-08	.030
rs2279308	17	74,306,576	A	.421	.020	.0038	9.6E-08	.420	.021	.0038	4.0E-08		.423	.019	.0038	3.3E-07	
rs4800452	18	18,981,609	T	.792	.048	.0047	4.2E-24	.785	.048	.0047	5.4E-24		.786	.048	.0047	5.4E-24	
rs12458127	18	44,911,356	T	.076	-.056	.0075	1.4E-13	.055	-.042	.0077	3.9E-08	.218	.057	-.043	.0077	2.8E-08	.211
rs9967417	18	45,213,498	C	.565	-.038	.0039	1.4E-22	.563	-.033	.0040	5.2E-17		.568	-.034	.0040	3.8E-17	
rs10871777	18	56,002,743	A	.761	-.025	.0044	3.1E-08	.765	-.025	.0044	2.3E-08		.759	-.025	.0044	2.3E-08	
rs12982744	19	2,128,193	C	.595	-.033	.0039	9.1E-17	.582	-.032	.0039	3.9E-16	-.012	.604	-.034	.0039	5.5E-18	.035
rs7507204	19	3,379,834	C	.247	.028	.0046	7.0E-10	.224	.027	.0046	4.6E-09	-.025	.237	.030	.0046	8.2E-11	.007
rs10413734	19	7,178,871	T	.672	-.024	.0042	1.8E-08	.674	-.023	.0042	4.6E-08	-.005	.669	-.024	.0042	8.0E-09	.009
rs4072910	19	8,550,031	C	.454	-.029	.0047	1.0E-09	.457	-.028	.0047	1.7E-09		.452	-.029	.0047	7.5E-10	
rs17318596	19	46,628,935	A	.370	.029	.0041	1.4E-12	.367	.029	.0041	1.5E-12		.373	.029	.0041	1.5E-12	
rs1741344	20	4,049,800	T	.631	-.026	.0040	4.1E-11	.640	-.026	.0040	4.7E-11	-.001	.591	-.027	.0040	3.5E-11	-.005
rs6140050	20	6,580,901	A	.650	-.039	.0040	4.4E-22	.644	-.039	.0040	1.8E-22		.629	-.039	.0040	1.4E-22	
rs7274811	20	31,796,842	T	.231	-.040	.0045	7.9E-19	.237	-.042	.0045	2.3E-20	.126	.263	-.042	.0046	3.3E-20	.138
rs6060154	20	33,063,262	A	.264	.023	.0042	5.9E-08	.278	.033	.0043	9.5E-15	.040	.302	.030	.0043	9.5E-13	-.006
rs143384	20	33,489,170	A	.581	-.064	.0041	2.5E-55	.595	-.053	.0044	4.5E-33	-.390	.597	-.052	.0044	8.2E-32	-.384
rs6060739	20	34,031,006	T	.188	.052	.0050	2.8E-25	.184	.032	.0054	2.4E-09		.178	.032	.0054	3.7E-09	
rs237743	20	47,336,426	A	.208	.034	.0046	1.7E-13	.219	.034	.0046	2.1E-13	.000	.222	.034	.0046	3.1E-13	.010
rs913000	20	54,269,761	T	.309	.024	.0041	1.3E-08	.300	.023	.0041	1.0E-08		.297	.023	.0041	1.5E-08	
rs2834442	21	34,612,656	A	.646	.027	.0039	5.0E-12	.659	.027	.0039	5.3E-12		.639	.027	.0039	5.3E-12	
rs4821083	22	31,386,341	T	.835	.033	.0051	6.3E-11	.850	.033	.0051	7.6E-11		.851	.033	.0051	7.6E-11	

**Supplementary Table 3** Summary of 33 BMI-associated SNPs with p-values < 5e-8 identified by the conditional and joint analysis using the ARIC cohort as reference sample with their effects replicated by a joint analysis using the QIMR cohort as reference sample. SNPs on different chromosome or more than 10Mb distant are assumed to be in linkage equilibrium. Chr, chromosome; A1, reference allele; Freq: frequency of the reference allele;  $\beta$ , marginal effect;  $b$ , joint effect;  $r$ , LD correlation between an associated SNP and the next adjacent associated SNP.

SNP	Chr	bp	A1	GIANT MA				Joint analysis with LD from ARIC					Joint analysis with LD from QIMR				
				Freq	$\beta$	s.e.	P	Freq	b	s.e.	P	r	Freq	b	s.e.	P	r
rs2815752	1	72,585,028	A	.611	.038	.0042	6.4E-19	.615	.038	.0042	2.6E-19	-.002	.615	.038	.0042	1.8E-19	-.007
rs1514177	1	74,763,990	C	.429	.029	.0041	3.7E-12	.426	.029	.0041	2.3E-12		.419	.029	.0041	1.6E-12	
rs11165643	1	96,696,685	T	.586	.024	.0042	1.4E-08	.585	.024	.0042	1.7E-08		.589	.024	.0042	1.7E-08	
rs543874	1	176,156,103	A	.810	-.044	.0052	2.2E-17	.803	-.044	.0052	1.6E-17		.794	-.044	.0052	1.6E-17	
rs2860323	2	604,210	A	.176	-.062	.0056	7.6E-29	.171	-.062	.0056	1.2E-28		.168	-.062	.0056	1.2E-28	
rs10182181	2	25,003,800	A	.538	-.025	.0041	2.0E-09	.537	-.025	.0041	1.7E-09		.509	-.025	.0041	1.7E-09	
rs17016663	2	79,347,442	C	.110	.039	.0066	6.0E-09	.106	.039	.0066	4.6E-09		.109	.039	.0066	4.6E-09	
rs2890652	2	142,676,401	T	.819	-.032	.0054	2.9E-09	.824	-.032	.0054	2.5E-09		.831	-.032	.0054	2.5E-09	
rs9826482	3	85,959,265	A	.200	.032	.0051	8.0E-10	.192	.032	.0051	6.6E-10		.200	.032	.0051	6.6E-10	
rs2640017	3	142,817,811	A	.937	-.047	.0085	2.5E-08	.936	-.047	.0085	2.5E-08		.933	-.047	.0085	2.5E-08	
rs9816226	3	187,317,193	A	.181	-.046	.0054	9.7E-18	.180	-.046	.0054	1.7E-17		.179	-.046	.0054	1.7E-17	
rs10938397	4	44,877,284	A	.569	-.042	.0043	5.8E-22	.571	-.042	.0043	4.0E-22		.563	-.042	.0043	4.0E-22	
rs13107325	4	103,407,732	T	.075	.056	.0093	1.6E-09	.092	.056	.0093	1.7E-09		.095	.056	.0093	1.7E-09	
rs1024980	5	62,867,357	T	.807	.029	.0052	2.1E-08	.801	.029	.0052	1.6E-08		.799	.029	.0052	1.6E-08	
rs2112347	5	75,050,998	T	.632	.027	.0042	3.3E-10	.617	.027	.0042	2.1E-10		.642	.027	.0042	2.1E-10	
rs4836133	5	124,360,002	A	.479	.024	.0043	1.1E-08	.501	.024	.0043	1.6E-08		.487	.024	.0043	1.6E-08	
rs987237	6	50,911,009	A	.817	-.049	.0053	2.6E-20	.817	-.049	.0053	1.4E-20		.817	-.049	.0053	1.4E-20	
rs6955651	7	76,477,807	T	.178	.049	.0088	3.7E-08	.148	.049	.0088	3.6E-08		.133	.049	.0088	3.6E-08	
rs2922763	8	76,736,266	T	.708	.027	.0046	2.6E-09	.713	.028	.0046	1.2E-09	-.024	.726	.027	.0046	4.4E-09	.016
rs1465809	8	85,243,012	A	.752	.026	.0048	1.3E-07	.762	.026	.0048	4.4E-08		.729	.025	.0048	1.6E-07	
rs10968576	9	28,404,339	A	.687	-.029	.0044	7.4E-11	.687	-.029	.0044	6.0E-11		.679	-.029	.0044	6.0E-11	
rs11191560	10	104,859,028	T	.911	-.036	.0073	1.2E-06	.912	-.036	.0073	1.2E-06		.920	-.036	.0073	1.2E-06	
rs7101471	11	8,420,198	A	.488	-.026	.0041	7.0E-10	.488	-.026	.0041	5.0E-10		.476	-.026	.0041	5.0E-10	
rs10767664	11	27,682,562	A	.785	.042	.0050	9.9E-17	.786	.042	.0050	6.4E-17		.791	.042	.0050	6.4E-17	
rs3817334	11	47,607,569	T	.407	.031	.0042	4.6E-14	.417	.031	.0042	7.7E-14		.407	.031	.0042	7.7E-14	
rs7138803	12	48,533,735	A	.380	.032	.0042	3.2E-14	.379	.032	.0042	1.8E-14		.371	.032	.0042	1.8E-14	
rs4771122	13	26,918,180	A	.763	-.030	.0050	1.5E-09	.783	-.030	.0050	2.0E-09		.775	-.030	.0050	2.0E-09	
rs11847697	14	29,584,863	T	.043	.073	.0111	4.8E-11	.044	.073	.0111	4.6E-11		.037	.073	.0111	4.6E-11	
rs17836088	14	79,001,794	C	.214	.030	.0050	2.8E-09	.219	.030	.0050	2.5E-09		.221	.030	.0050	2.5E-09	
rs2241423	15	65,873,892	A	.215	-.037	.0050	1.4E-13	.233	-.037	.0050	1.9E-13		.208	-.037	.0050	1.9E-13	
rs12444979	16	19,841,101	T	.133	-.046	.0061	4.1E-14	.140	-.045	.0061	1.0E-13	.014	.145	-.047	.0061	1.5E-14	-.020
rs7498665	16	28,790,742	A	.596	-.031	.0042	1.9E-13	.599	-.030	.0042	4.8E-13		.609	-.031	.0042	7.1E-14	
rs1558902	16	52,361,075	A	.416	.080	.0042	1.9E-81	.413	.080	.0042	4.7E-81		.395	.080	.0042	4.7E-81	

**Supplementary Table 4** Comparison between the actual and approximate conditional analyses with a reference sample of 6,654 randomly sampled from the discovery set. The simulation method and scheme can be found in **Supplementary Note**.

SNP	Parameter			Single SNP MA of 46 cohorts ( $n = 130,000$ )				Actual Cond.		Cond. MA		Approximate Cond.			
	$b$	$p$	$r$	$^{\$} f$	$^{\$} r$	$b$	p-value	$b$	$P$	$b$	p-value	$^{\#} f$	$b$	p-value	$^{\#} r$
1_1	0.06	0.2	-0.4	0.202 (0.160, 0.280)	-0.391 (-0.436, -0.357)	-0.046	1.2E-20	-0.057	3.0E-27	-0.058	1.1E-27	0.183	-0.058	1.1E-27	-0.379
1_2	-0.025	0.4		0.405 (0.338, 0.466)		-0.007	6.2E-02	-0.025	3.8E-09	-0.026	2.7E-09	0.401	-0.025	4.6E-09	
2_1	0.04	0.2	0.2	0.209 (0.134, 0.281)	0.202 (0.148, 0.303)	0.055	4.2E-30	0.046	3.7E-21	0.047	3.5E-21	0.170	0.047	3.4E-21	0.205
2_2	0.05	0.15		0.146 (0.076, 0.209)		0.060	3.0E-27	0.049	3.6E-18	0.049	4.2E-18	0.142	0.049	5.7E-18	
3_1	-0.04	0.15	0.0	0.157 (0.077, 0.233)	-0.001 (-0.052, 0.079)	-0.033	1.1E-09	-0.033	1.5E-09	-0.033	1.2E-09	0.153	-0.034	3.3E-10	0.017
3_2	0.03	0.2		0.202 (0.134, 0.261)		0.030	7.6E-10	0.030	9.4E-10	0.030	8.5E-10	0.186	0.031	3.0E-10	

<sup>\$</sup> mean (range) of frequencies and LD correlations observed in the discovery set of 46 cohorts; <sup>#</sup> estimates of frequency and LD correlation in the reference sample; Cond.: conditional analysis.

**Supplementary Table 5** Nine loci with multiple associated SNPs for BMI with p-values < 5e-6 identified by the conditional and joint analysis with LD estimated from the ARIC cohort. SNPs on different chromosome or more than 10Mb distant are assumed to be in linkage equilibrium. Chr, chromosome; A1, reference allele; Freq: frequency of the reference allele;  $\beta$ , marginal effect;  $b$ , joint effect;  $r$ , LD correlation between an associated SNP and the next adjacent associated SNP.

SNP	Chr	bp	Nearest gene	A1	GIANT MA				Joint analysis with LD from ARIC				
					Freq	$\beta$	s.e.	P	Freq	b	s.e.	P	r
rs6548221	2	285,255	FAM150B	A	.215	.022	.0050	8.1E-06	.219	.023	.0050	2.9E-06	.018
rs2860323	2	604,210	TMEM18	A	.176	-.062	.0056	7.6E-29	.171	-.063	.0056	5.0E-29	
rs12636352	3	186,952,372	IGF2BP2	A	.372	.020	.0045	9.6E-06	.361	.021	.0045	2.7E-06	.027
rs9816226	3	187,317,193	ETV5	A	.181	-.046	.0054	9.7E-18	.180	-.047	.0054	5.9E-18	
rs2281820	6	33,876,875	MLN	A	.426	-.018	.0041	1.7E-05	.419	-.020	.0041	1.8E-06	-.001
rs9296115	6	34,542,693	PACSIN1	A	.791	-.028	.0052	6.6E-08	.799	-.027	.0052	1.3E-07	
rs1331903	9	28,388,636	LINGO2	T	.321	.011	.0044	1.7E-02	.322	.024	.0047	4.5E-07	.348
rs10968576	9	28,404,339	LINGO2	A	.687	-.029	.0044	7.4E-11	.687	-.037	.0047	2.0E-15	
rs2275241	9	128,410,397	LMX1B	A	.370	.023	.0043	1.8E-07	.359	.021	.0043	8.5E-07	-.080
rs867559	9	128,505,146	LMX1B	A	.783	-.028	.0052	6.0E-08	.801	-.025	.0052	2.0E-06	
rs2877960	14	28,798,754	PRKD1	A	.358	-.021	.0043	1.4E-06	.347	-.020	.0043	2.5E-06	-.017
rs11847697	14	29,584,863	PRKD1	T	.043	.073	.0111	4.8E-11	.044	.072	.0111	7.6E-11	
rs6499640	16	52,327,178	FTO	A	.613	.042	.0045	1.2E-20	.612	.023	.0046	1.1E-06	.256
rs1558902	16	52,361,075	FTO	A	.416	.080	.0042	1.9E-81	.413	.075	.0043	3.0E-67	
rs12939549	17	76,226,319	KIAA1303	A	.567	.021	.0041	2.7E-07	.562	.022	.0041	1.0E-07	.034
rs4076427	17	76,702,132	BAIAP2	C	.392	-.023	.0047	9.1E-07	.400	-.024	.0047	3.5E-07	
rs6567160	18	55,980,115	MC4R	T	.762	-.055	.0049	3.7E-29	.767	-.046	.0051	3.5E-19	.292
rs9675886	18	56,120,302	MC4R	A	.718	-.037	.0045	3.1E-16	.717	-.024	.0047	3.8E-07	.072
rs7227255	18	56,206,711	MC4R	A	.024	-.097	.0157	7.4E-10	.021	-.082	.0158	1.8E-07	

## Supplementary Note

### Simulation study

We mimicked the GIANT MA by a simulation study of 46 cohorts with a total sample size of 130,000. We generated the genotypes of a pair of SNPs in each cohort from a bivariate binomial distribution<sup>3</sup> given their allele frequencies and LD correlation,

i.e.  $\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} \sim B(f_1, f_2, r)$ , where the subscripts “1” and “2” represent the two SNPs,  $x$  is the genotype indicator variable with value of 0, 1 or 2,  $f$  is the allele frequency and  $r$  is the LD correlation. The sample size ( $n_i$ ) of each cohort was drawn from a normal distribution with mean of 3000 and SD of 3000, i.e.  $n_i \sim N(3000, 3000)$ , with constraints that  $n_i \geq 500$  and  $\sum_i^{46} n_i = 130,000$ . The allele frequency of a SNP was allowed to vary across cohorts, i.e. for the  $i$ -th cohort,  $f_{1(i)} \sim N(p_1, 0.03)$  and  $f_{2(i)} \sim N(p_2, 0.03)$ . We generated the phenotypes in each cohort using a two-locus model  $y = x_1 b_1 + x_2 b_2 + e$ , where  $b_1$  and  $b_2$  are the effect sizes and  $e$  is the residual effect with  $e \sim N(0, 1)$ , and standardized them to z-scores. We performed association analyses of the SNPs in each cohort and combined the results of all cohorts using the inverse-variance meta-analysis method. We then randomly sampled  $m = 6,654$  ‘individuals’ from the simulated discovery sample as the reference sample to perform the approximate conditional analysis (Online Methods). For comparisons, we performed the “actual conditional analysis” using the pooled individual-level genotype data of the whole discovery sample and the “conditional MA” i.e. combining results from the conditional analyses in individual cohorts. We simulated three pairs of SNPs under the following scenarios that represent examples we observed from the real data analysis (Table 1 in the main text). The increasing alleles of two SNPs are

- I) negatively correlated (SNPs 1\_1 and 1\_2);
- II) positively correlated (SNPs 2\_1 and 2\_2);
- III) uncorrelated (SNPs 3\_1 and 3\_2).

We show in the **Supplementary Table 4** that in all three scenarios the results from the actual and approximate conditional are very similar. We repeated the simulation 1,000 times and plotted the p-values from the conditional MA against those from the approximate conditional analysis. It is shown in **Supplementary Figure 3** that p-values from the approximate conditional analysis are highly consistent with those from the actual conditional MA ( $R^2 > 0.98$ ) in all three scenarios, suggesting that the proposed method approximates the conditional MA with high precision. In order to quantify the size of the reference sample that is required to get precise approximation of the actual conditional analysis, we repeated the simulation for 1,000 times and correlated the p-values from the actual conditional analysis with those from the approximate conditional analysis for a range of sizes of reference samples. It is shown in **Supplementary Figure 4** that a reference sample with a size of at least 2,000 is required and a size of larger than 5,000 is recommended. We also show that the results are basically unchanged even if the reference sample is independent of the discovery set, as long as both are from the same general population (**Supplementary Figure 4**).

### **Multiple associated SNPs at a locus are unlikely to be in LD with a single causal variant**

Define  $\beta_1$  and  $\beta_2$  as the marginal effects of two SNPs and define  $h_1 = 2p_1(1 - p_1)$  and  $h_2 = 2p_2(1 - p_2)$  with  $p_1$  and  $p_2$  being the MAF of the two SNPs. Assuming that these two SNPs are in LD with a single causal variant with effect size of  $\beta_0$  and MAF of  $p_0$ ,

$$\beta_1 = \beta_0 r_{01} \sqrt{h_0 / h_1}$$

$$\beta_2 = \beta_0 r_{02} \sqrt{h_0 / h_2}$$

where  $r_{01}$  and  $r_{02}$  are the LD correlations between the two SNPs and the causal variant, respectively, and  $h_0 = 2p_0(1 - p_0)$ . Therefore, the ratio between the two LD correlations is

$$r_{01}/r_{02} = \beta_1\sqrt{h_1}/\beta_2\sqrt{h_2}$$

Given the MAF of the two SNPs and that of the causal variant, the upper limits of  $r_{01}^2$  and  $r_{02}^2$  are<sup>4</sup>

$$r_{01(\max)}^2 = p_0(1 - p_0 - v_{01})/[(1 - p_0)(p_0 + v_{01})]$$

$$r_{02(\max)}^2 = p_0(1 - p_0 - v_{02})/[(1 - p_0)(p_0 + v_{02})]$$

where  $v_{01} = |p_1 - p_0|$  and  $v_{02} = |p_2 - p_0|$ .

If we model the two SNPs simultaneously, their joint effects are

$$b_1 = \beta_0\sqrt{h_0/h_1}(r_{01} - r_{02}r_{12})$$

$$b_2 = \beta_0\sqrt{h_0/h_2}(r_{02} - r_{01}r_{12})$$

where  $r_{12}$  is the LD correlation between the two SNPs.

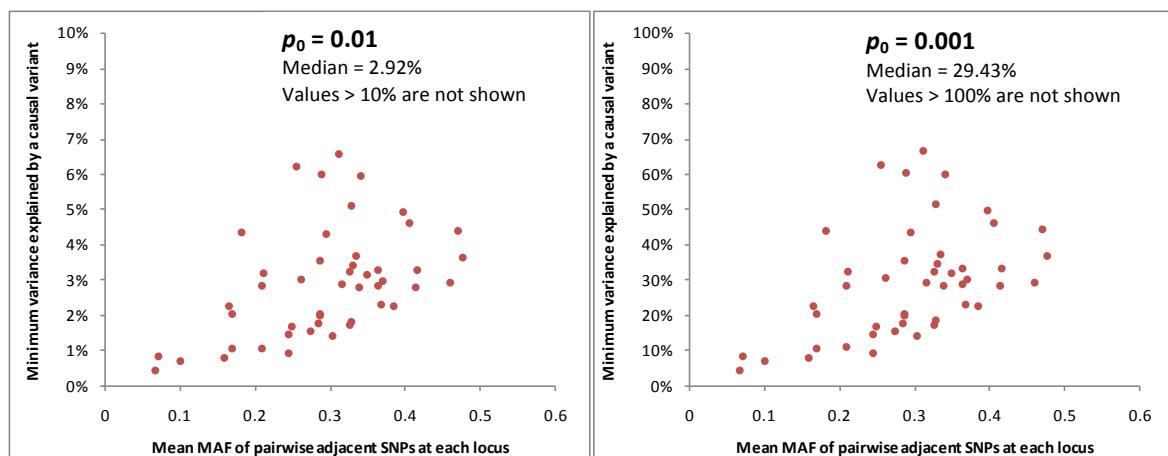
Under the assumption that the a pair of multiple associated SNPs at a locus are in LD with a single causal variant, we can calculate the minimum effect size of the causal variant that is required to generate the observed effects of the SNP markers by the following procedure:

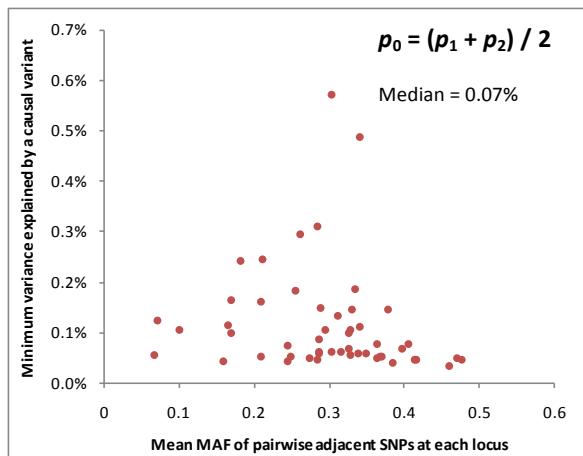
- 1) Calculate  $r_{02} = r_{02(\max)} = \sqrt{p_0(1 - p_0 - v_{02})/[(1 - p_0)(p_0 + v_{02})]}$  given a value of  $p_0$ . For simplicity, here we assume that  $r_{02}$  is positive (the result will be the same if we assume it is negative).
- 2) Calculate  $r_{01} = r_{02}\beta_1\sqrt{h_1}/\beta_2\sqrt{h_2}$ . If  $r_{01}^2$  is larger than  $r_{01(\max)}^2$ , both  $r_{01}$  and  $r_{02}$  are adjusted by a factor of  $\sqrt{r_{01(\max)}^2}/|r_{02(\max)}\beta_1\sqrt{h_1}/\beta_2\sqrt{h_2}|$ .

3) Calculate the minimum variance explained by the causal variant required to generate the observed SNP effects  $q_{0(\min)}^2 = h_0\beta_{0(\min)}^2 = \max[h_1 b_1^2 / (r_{01} - r_{02} r_{12})^2, h_2 b_2^2 / (r_{02} - r_{01} r_{12})^2]$

We calculated  $q_{0(\min)}^2$  for each pair of adjacent SNPs at the 36 loci that have multiple associated SNPs with height under two different assumptions: 1) the causal variants are rare with MAF of 0.01, 0.001 and 0.0001; 2) the causal variants are common with MAF of  $(p_1 + p_2) / 2$ .

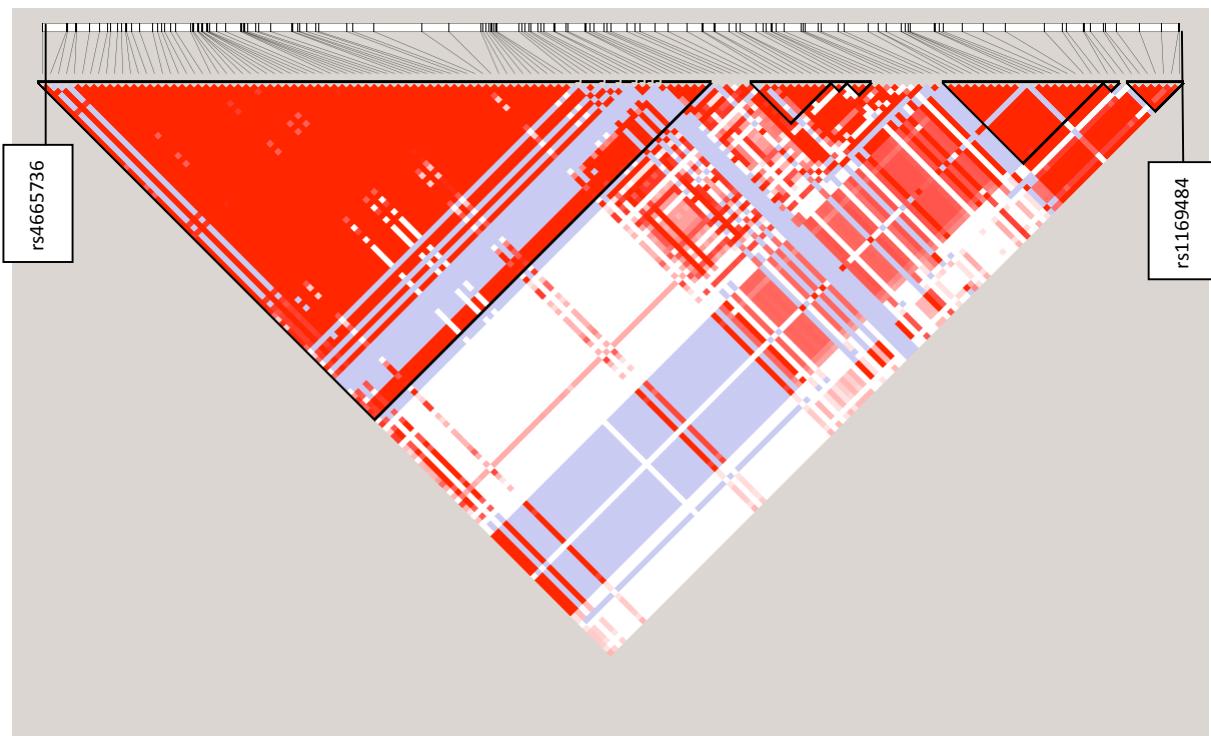
We show in the following figures that it is unlikely that the adjacent multiple associated SNPs are caused by single causal variants especially for the SNPs with MAF > 0.1 because otherwise the sum of variance explained over all the 36 loci is greater than the heritability of height (80%), and that it is theoretically possible that the single causal variants are common.





In practice, however, it is implausible that a common causal variant is not well tagged by a genotyped or imputed SNP nearby but by two SNPs in different haplotype blocks. For example, SNPs rs4665736 and rs11694842, which are jointly significant (see table below), are located in two distinct haplotype blocks. It seems highly unlikely that these two SNPs are in LD with a single causal variant somewhere in this region according to the LD pattern illustrated in the figure below.

SNP	Chr	bp	Nearest gene	A1	GIANT single SNP MA				Joint analysis, LD from ARIC cohort				
					Freq	b	P	$q_L^2$ (%)	Freq	b	P	r	$q^2$ (%)
rs4665736	2	25,041,103	RBJ	T	0.535	0.034	1.3E-18	0.058	0.533	0.029	3.7E-14	0.123	0.050
rs11694842	2	25,336,474	DNMT3A	A	0.669	0.028	2.6E-12		0.660	0.026	1.1E-10		0.033



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